

**REMARKS**

Claims 56, 57, 60-63, 65-68 and 70-78 were previously pending. Claim 67 has been canceled and claim 68 has been amended. Accordingly, claims 56, 57, 60-63, 65, 66, 68 and 70-78 are presented for examination. Reconsideration is requested.

**I. THE OCTOBER 26, 2005 INTERVIEW**

Applicant sincerely thanks the Examiners for the courtesies graciously extended during the interview held at the Patent and Trademark Office on October 26, 2005 between the inventor, his undersigned representative, and Examiners Srivastava and Gitomer. The pending claims, objections, rejections, and the cited Dev '710 and Bini '322 patents were discussed.

Applicant explained that the presently claimed methods require that the treatment result in enlargement of the diameter of the treated artery or vein itself, not merely enlargement of the diameter of the lumen. By the methods of the present invention, an obstructed or stenosed blood vessel can be enlarged while optionally avoiding dilation by means of a mechanical device such as a transluminal balloon catheter, which is known to damage the vascular endothelium. At the discretion of the treating physician, treatment in accordance with the presently claimed methods can include or exclude the use of such a device. The present invention further provides for prophylactic therapy of an artery or vein, even before obstruction, stenosis, or intimal hyperplasia is manifest.

Applicant submitted that prior to the present invention, the art taught away from elastase treatment of a blood vessel in a human subject at a dose sufficient to enlarge the diameter of the treated vessel, which had been used in animals to reproduce vessel pathology (aneurysm), but was considered unsuitable for human therapy. It is the present invention that for the first time teaches treating a blood vessel in a human subject with a dose of elastase sufficient to enlarge the diameter of the treated vessel, and teaches the use of a dose ranging study to determine an

optimal dose (*see* Specification, *e.g.* at page 15, lines 22-25), as is exemplified in the Franano Declaration of record.

Applicant pointed out that Dev '710 is concerned with the use of electroporation to permeabilize the endothelial layer of a blood vessel in order to enhance delivery of medicaments to the vessel wall, and does not refer to enlarging the diameter of a treated blood vessel; that low dose elastase can be used (as taught by Maillard) to enhance delivery of medicaments through the internal elastic lamina without enlarging the diameter of a treated blood vessel; and that it would be logical to combine electroporation (as taught by Dev '710) with a non-dilating low dose of elastase (as taught by Maillard) in order to enhance delivery of medicaments through the endothelium and internal elastic lamina into the subjacent layers of the blood vessel wall. Since the teachings of Dev '710 can be followed without enlarging the diameter of the treated blood vessel, Applicant submitted that Dev '710 does not inherently anticipate the pending claims.

Applicant further pointed out that Bini '322 is concerned with the use of a metalloproteinase to achieve fibrinolysis; that Bini '322 does not refer to enlarging the diameter of an artery or vein; and that metalloproteinases (including those identified by Bini '322 as having incidental elastase activity) can be used for fibrinolysis (as taught by Bini '322) at doses that do not cause enlargement of the diameter of a treated artery or vein. Since the teachings of Bini '322 can be followed without enlarging the diameter of a treated blood vessel, Applicant submitted that Bini '322 does not inherently anticipate the pending claims.

Since neither Dev '710 nor Bini '322 teaches or suggests administering elastase at a dose that leads to enlargement of the diameter of an artery or vein, Applicant submitted that, even if *arguendo* Dev '710 and Bini '322 were combined, such combination would not render obvious the presently claimed methods.

The objections to the specification and non-prior art claim rejections were also discussed. It was agreed that Applicant would amend the specification and claim 68 and would cancel claim 67, without prejudice, in order to expedite allowance.

## **II. OBJECTIONS TO THE SPECIFICATION**

In accordance with the Examiner's suggestion, the specification has been amended to delete the word "targets" where it was inadvertently added in correcting typographical errors in the paragraph at page 7, lines 19-28. The word "agents" has been restored as recited at page 7, line 19 of the originally filed specification.

Applicant respectfully submits that the phrase "at least about 20%" appears at page 11, line 24 of the specification as originally filed, and accordingly does not constitute new matter in the amended text submitted at page 6, line 8 of the Reply filed on May 17, 2005.

## **III. REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

Claim 67 was rejected under 35 U.S.C. § 112, second paragraph, on the grounds that the recitation of the word "isolated" makes the claim vague and unclear. Applicant respectfully submits that the term "isolated" has a clear and definite meaning to one of skill in the art in the context of the present invention. Nevertheless, in order to expedite allowance, Applicant has now cancelled claim 67, thereby obviating the rejection, without prejudice to the right to present the presently cancelled subject matter in a continuing application.

Claim 68 was rejected under 35 U.S.C. § 112, second paragraph, as indefinite for reciting the word "selected." Claim 68 has been amended to remove that recitation, thereby obviating the rejection.

Claim 78 was rejected as being in improper form, since a multiple dependent claim should refer to other claims in the alternative only, and cannot depend from any other multiple dependent claim. Applicant respectfully points out that claim 78 refers to other claims in the alternative by using the word "or" and further that claim 78 does not depend from any other claim that is multiple dependent. Specifically, claim 78 depends from claims 70-77. Claim 70 is an independent claim; claim 71 depends solely from claim 70; claim 72 depends solely from claim 71; claim 73 depends solely from claim 70; and claim 74 depends solely from claim 73. Likewise, claim 75 is an independent claim; claim 76 depends solely from claim 75; and claim

77 depends solely from claim 76. Thus, each of claims 70-77 is singular dependent.

Accordingly, Applicant submits that claim 78 is in proper form.

#### **IV. REJECTIONS UNDER 35 U.S.C. § 102**

##### **A. Rejection Over Dev '710**

Claims 56-63, 65 and 67-68 were rejected under 35 U.S.C. § 102(a) as anticipated by U.S. Patent No. 5,944,710 to Dev *et al.* ("Dev '710").

As submitted during the October 26, 2005 interview, Dev '710 is concerned with the use of electroporation to permeabilize the endothelial layer of a blood vessel in order to enhance delivery of medicaments to the vessel wall, and does not refer to enlarging the diameter of a treated blood vessel. Low dose elastase can be used (as taught by Maillard) to enhance delivery of medicaments through the internal elastic lamina without enlarging the diameter of a treated blood vessel. Accordingly, it would be logical to combine electroporation (as taught by Dev '710) with a non-dilating low dose of elastase (as taught by Maillard) in order to enhance delivery of medicaments through the endothelium and internal elastic lamina into the subjacent layers of the blood vessel wall. Applicant further refers to, and incorporates by reference, the discussion and remarks at pages 22-26 of the Reply filed on May 17, 2005.

Since the teachings of Dev '710 can be followed without enlarging the diameter of the treated blood vessel, it follows that Dev '710 does not inherently anticipate the pending claims. Accordingly, the rejection under § 102(a) over Dev '710 should be withdrawn.

##### **B. Rejection Over Bini '322**

Claims 56, 60-61, 65 and 67 were rejected under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,922,322 ("Bini '322").

As submitted during the October 26, 2005 interview, Bini '322 is concerned with the use of a metalloproteinase to achieve fibrinolysis. Bini '322 does not refer to enlarging the diameter of an artery or vein. Metalloproteinases (including those identified by Bini '322 as having

incidental elastase activity) can be used for fibrinolysis (as taught by Bini '322) at doses that do not cause enlargement of the diameter of a treated artery or vein.

Since the teachings of Bini '322 can be followed without enlarging the diameter of a treated blood vessel, it follows that Bini '322 does not inherently anticipate the pending claims. Accordingly, the rejection under § 102(a) over Bini '322 should be withdrawn.

**V. REJECTIONS UNDER 35 U.S.C. § 103(a)**

Claims 56-57, 60-63, 65-68 and 70-78 were rejected under 35 U.S.C. § 103(a) as obvious over Bini '322 in view of Dev '710.

As submitted during the October 26, 2005 interview, neither Dev '710 nor Bini '322 teaches or suggests administering elastase so as to cause enlargement of the diameter of a treated artery or vein, as required by the pending claims. Accordingly, even if *arguendo* Dev '710 and Bini '322 were combined, such combination would not render obvious the presently claimed methods.

**CONCLUSION**

In light of the above remarks, Applicant respectfully requests that the Examiner enter this Amendment After Final and allow the claims as herein amended. The Examiner is invited to call the undersigned attorney (212) 859-8973 if that would be helpful in resolving any remaining issues.

Date: November 3, 2005

Respectfully submitted,



40,286

Stephen S. Rabinowitz (Reg. No.)  
**FRIED, FRANK, HARRIS, SHRIVER**  
**& JACOBSON LLP**  
One New York Plaza  
New York, New York 10004  
(212) 859-8973